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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,909	10/13/2005	Yingxian Xiao	132848-01US	6970
50659	7590	04/02/2008		
Thomas Moga Butzel Long STONERIDGE WEST 41000 WOODWARD AVENUE BLOOMFIELD HILLS, MI 48304			EXAMINER ZARA, JANE J	
			ART UNIT 1635	PAPER NUMBER
			NOTIFICATION DATE 04/02/2008	DELIVERY MODE ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ball@butzel.com
patent@butzel.com
burns@butzel.com

Office Action Summary	Application No. 10/552,909	Applicant(s) XIAO ET AL.	
	Examiner Jane Zara	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 January 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5,8,9,13 and 15-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5,8,9,13 and 15-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>3-29-06</u> . | 6) <input checked="" type="checkbox"/> Other: <u>Seq. Compliance Notice</u> . |

DETAILED ACTION

This Office action is in response to the communication filed 1-7-08.

Claims 1-5, 8, 9, 13, 15-20 are pending in the instant application.

Election/Restrictions

Claims 10, 12 and 14 have been canceled and are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 1-7-08.

Applicant's election without traverse of Group I, claims 1-9, 11 and 13 and new claims 15-20 in the reply filed on 1-7-08 is acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13, 19 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 13, 19 and 20, in line 3, recite the parenthetical examples "(e.g. DNA, RNA, proteins or any other forms of molecules)." The metes and bounds of what is being claimed cannot be determined using these parenthetical, open ended examples.

Appropriate clarification is required.

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8, 9, 13, 15-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to nucleic acid constructs comprising a Type I Pol III promoter and further comprising *a sequence for generating a full or part of an RNA molecule which may bind its targets and regulate functions of targets, which targets include DNA, RNA, proteins or any other forms of molecules.*

Concise structural features that could distinguish structures within the expansive genus comprising sequences for generating a full or part of an RNA molecule which may bind its targets and regulate functions of targets, which targets include DNA, RNA, proteins or any other forms of molecules, from others are missing from the disclosure. No common structural attributes identify the members of this very broad claimed genus, and distinguish members within the claimed genus from those outside of the claimed genus.

The specification, claims and the art do not adequately describe the distinguishing features or attributes concisely shared by the members of the broad

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genus comprising *any sequence for generating a full or part of an RNA molecule which may bind its targets and regulate functions of targets, which targets include DNA, RNA, proteins or any other forms of molecules*. The specification teaches expression vectors comprising a Type I Pol III promoter operably linked to siRNA molecules.

The broad genus of nucleic acids claimed encompasses a myriad of structures (e.g. thousands of nucleic acid sequences) and the specification and claims do not adequately teach a representative number of species for the broad genus claimed (What exactly is embraced by RNA molecules that regulate functions of DNA, RNA, proteins or any other forms of molecules?).

One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe this expansive genus claimed. Thus, Applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-5, 8, 11, 13, 15-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Streb et al (US 2006/0122381).

Streb et al (US 2006/0122381) teach recombinant nucleic acid constructs comprising expression or cloning vectors comprising a native or engineered Type I Pol III promoter, and further comprising DNA encoding an RNA molecule which downregulates the expression of a target gene, which RNA molecule optionally comprises siRNA, antisense, ribozymes or aptamers (see. page 3, paragraphs 0030 – page 6, paragraph 0051; page 7, paragraph 0064- page 9, paragraph 0074; page 11, paragraph 0103-page 14, paragraph 0138).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 8, 9, 13, 15-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Streb et al (US 2006/0122381) as applied to claims 1-5, 8, 11, 13, 15-20 above, and further in view of Beach (US 2003/0084471).

The claims are drawn to recombinant nucleic acid constructs comprising expression or cloning vectors comprising a native or engineered Type I Pol III promoter and further comprising DNA encoding an RNA molecule which downregulates the expression of a target gene, which target gene comprises a mammalian or a viral gene.

Streb is relied upon as cited in the 102 rejection above.

Streb does not teach targeting mammalian or viral genomic genes using siRNA.

Beach et al (2003/0084471) teach expression vectors comprising Pol III promoters operably linked to siRNA, which siRNA targets and inhibits the expression of target mammalian and viral genome genes (see esp. pages 1-3; page 9; pages 12-13. At paragraphs 0251-2), Beach teaches the advantages of expressing siRNA using expression vectors comprising Pol III promoters "An object of the present invention is to improve methods for generating siRNAs and short hairpins for use in specifically suppressing gene expression. Example 6 demonstrates that siRNAs and short hairpins are highly effective in specifically suppressing gene expression. Accordingly, it would be advantageous to combine the efficient suppression of gene expression attainable using short hairpins and siRNAs with a method to encode such RNA on a plasmid and express it either transiently or stably. ... FIG. 42 demonstrates that short hairpins encoded on a plasmid are effective in suppressing gene expression. DNA oligonucleotides encoding 29 nucleotide hairpins corresponding to firefly luciferase were

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inserted into a vector containing the U6 promoter. Three independent constructs were examined for their ability to specifically suppress firefly luciferase gene expression in 293T cells. Beach et al at paragraph 0253 teach: "The results summarized in FIG. 42 demonstrate that transient expression of siRNAs and short hairpins encoded on a plasmid can efficiently suppress gene expression. One of skill can choose from amongst a range of vectors to either transiently or stably express an siRNA or short hairpin."

It would have been obvious to one of ordinary skill in the art to design expression or cloning vectors comprising Type I Pol III promoters for expression of inhibitory constructs, including siRNA, because these expression constructs were known in the art at the time the invention was made, as taught previously by Streb. One of ordinary skill in the art would have been motivated to use this promoter type because Streb taught the ability of this promoter to drive expression of operably linked, downstream RNA constructs in a suitable expression vector, and the essential elements of Type I Pol III promoters was well known in the art, and was successfully engineered to drive expression in recombinant vectors. One of ordinary skill in the art would have been motivated to target viral genes because inhibiting the expression of viral genomic genes was well known in the art to prevent expression of viral target genes required for viral infectivity and replication, and inhibiting the expression of these previously identified viral genes would reasonably be expected to reduce viral infectivity and replication. One would be motivated to target portions of mammalian genome with inhibitory molecules expressed from the instantly claimed nucleic acid constructs in

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order to investigate the functions of a particular mammalian genome segment. One of ordinary skill in the art would have reasonably expected that using the instantly claimed constructs would lead to inhibition of target gene expression.

One of ordinary skill in the art would have expected that these retroviral constructs would provide for the expression of dsRNA molecules for the targeting and inhibition of a target gene because the expression of RNA constructs downstream of the polymerase promoter was taught previously in the art by many, as evidenced by the teachings of Beach and Streb.

For these reasons, the instant invention would have been obvious to one of ordinary skill in the art.

Sequence Compliance Notice

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. **Please provide accompanying SEQ ID Nos. where appropriate for the nucleic acid sequences disclosed in the figures and the specification (see, e.g. the specification at pages 8-9).** See the accompanying Notice to Comply.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. ' 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jane Zara whose telephone number is (571) 272-0765. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz, can be reached on (571) 272-0763. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jane Zara

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/Jane Zara/

Primary Examiner, Art Unit 1635